applications claiming the canceled subject matter and the claim cancellations should not be construed as abandonment or agreement with the Examiner's position in the Office Action.

Applicants note that 29-36, 38-55, and 57-60 are withdrawn pursuant to an election of species. Applicants recognize that, per MPEP §809.02(c), to the extent all species fall within the limitations of a generic claim ultimately determined to be patentable, the non-elected species will no longer be deemed to be withdrawn and claims to the additional non-elected species will be considered by the Examiner.

Change in correspondence address.

Applicants note that a Revocation and Substitute Power of Attorney incorporating a change in correspondence address was filed on May 3, 2001, a copy of which is enclosed. In accordance with the instructions provided on May 3, 2001, **please direct all future correspondence regarding the subject application to CUSTOMER NUMBER 22798, that is:**

22798

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35 U.S.C. §112, Second Paragraph, New Rejection.

Claims 26-28, 37, 56, and 61-63 were rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite because claim 26 allegedly lacked a necessary step to correlate the result with the preamble. Applicants have amended claim 26, herein to expressly recite:

> ". . . detecting the formation of a hybridization complex to determine **the relative copy number of a nucleic acid in chromosomal region 20q13.2, thereby identifying** the presence or absence of neoplastic cells having an increased copy number of nucleic acid sequences at chromosomal region 20q13.2."

The claim, as amended, expressly relates back to the preamble which states:

> "26. A method of detecting in a sample the presence or absence of neoplastic cells having an increased copy number of nucleic acid sequences at chromosome region 20q13.2, the method comprising:. . . "

The steps of amended claim 26 clearly relate back to the preamble and this rejection under 35 U.S.C. §112, second paragraph, should therefore be withdrawn.

35 U.S.C. §112, First Paragraph, New Matter, New Rejection.

Claims 26-28, 37, 56, and 61-63 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification. In particular, the Examiner alleged that claims 26-28, 37, 56, and 61-63 were drawn to a method for detecting the "absence" of cancer in a sample having an increased copy number of nucleic acid sequences at chromosome region 20q13.2 and argued that the specification does not contemplate a method of detecting the absence of cancer in a sample having an increased copy number of nucleic acid sequences at the recited chromosomal region. Applicants traverse by argument and amendment.

Applicants respectfully suggest that the Examiner has misread the preamble. The phrase "having an increased copy number" was intended to refer to the word cells rather than to the word "sample". Nevertheless, for clarity, Applicants have amended the preamble herein to recite:

> "26. A method of detecting in a sample the presence or absence of neoplastic cells having an increased copy number of nucleic acid sequences at chromosome region 20q13.2, the method comprising:. . . "

In view of this amendment it is clear that the phrase "having an increased copy number" refers to neoplastic cells rather than to the sample. Accordingly this rejection under 35 U.S.C. §112, first paragraph, should be withdrawn.

35 U.S.C. §112, First Paragraph, Enablement, New Rejection.

Claims 26-28, 37, 56, and 61-63 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to enable one skill in the art to make or sue the invention. Similar to the "new matter" rejection, the Examiner alleged that it is not clear how one could determine the absence of cancer in a sample having an increased copy number of nucleic acid sequences at chromosome 20q13.2. Applicants traverse.

As noted above, Applicants have amended the preamble of claim 26, so that it is clear that the phrase "having an increased copy number" refers to neoplastic cells rather than to the sample. According Accordingly the pending claims are drawn to a method of detecting the presence or absence

of neoplastic cells having an increased copy number, rather than a method of detecting neoplastic cells in a sample having an increased copy number.

Accordingly, the rejection of claims 26-28, 37, 56, and 61-63 under 35 U.S.C. §112, first paragraph, on these grounds should be withdrawn.

35 U.S.C. §112, First Paragraph, Written Description, New Rejection.

Claims 26 and 37 were rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to meet the description requirement. The Examiner alleged that the "genus" of probes allegedly recited in claims 26 and 37 was not adequately described in the specification and cites The Regents of the *University of California v Eli Lilly*, 43 USPQ2d 1398-1412 in support of this position. Applicants respectfully traverse.

The Examiner is reminded that "[t]he written description requirement **does not require the applicant 'to describe exactly the subject matter claimed**, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. [emphasis added] '" *Union Oil Co. v Atlantic Richfield et al.* 208 F.3d 989 (Fed. Cir. 2000) *citing In re Gosteli*, 872 F.2d 1008, 1012, 10 U.S.P.Q.2D (BNA) 1614, 1618 (Fed. Cir. 1989).

In the present case, independent claim 26 expressly recites:

> [C]ontacting a nucleic acid sample from a human patient with a probe which **hybridizes to a target polynucleotide sequence under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes, the target polynucleotide sequence comprising a sequence selected from the group consisting of** SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, **SEQ ID NO:9**, . . . [emphasis added]

There is simply no question that the specification, as filed, communicates to one of ordinary skill in the art that Applicants invented what is claimed. As stated by the Federal Circuit in *Union Oil:*

> If lack of literal support alone were enough to support a rejection under §112, then the statement of In re Lukach. . . that "the invention claimed does not have to be described in ipsis verbis in order to satisfy the description requirement of §112, is empty verbiage.

Thus, literal language describing every claimed species is not required to meet the description requirement. To the contrary, as evidenced in *Union Oil*, guidelines and functional descriptions leading one of skill to the claimed invention are sufficient to meet the description requirements.

In the present case, the specification provides more than guidelines and functional descriptions. Particular reference nucleic acid sequences are provided. Stringent hybridization conditions are defined and recited in the claim. Numerous sequences meeting the limitations of claim 26 readily identified by one of ordinary skill in the art. One of ordinary skill in the art would readily appreciate that Applicants were "in possession" of the claimed invention. Accordingly, the rejection of claims 26-28, 37, 56, and 61-63 under 35 U.S.C. §112, first paragraph, description requirement should be withdrawn.

35 U.S.C. §112, First Paragraph, Enablement.

Claims 26, 28, 37, 56, and 61-63 were rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabled. The Examiner alleged that the claims are not enabled because they are directed to detecting any type of cancer and the amplified region identified in the present application is not necessarily associated with any type of cancer. Applicants respectfully traverse.

In making her rejection, the Examiner implicitly reads a limitation into the claims that is not present. In particular, by arguing that the claims are not enabled because there exist cancers that do not comprise amplifications at 20q13.2 the Examiner improperly reads the claims as requiring the diagnosis of any and all cancers, including those lacking the recited amplifications.. This simply is not the case.

The claims are directed to a method of detecting "the presence or absence of **neoplastic cells having an increased copy number of nucleic acid sequences at chromosome region 20q13.2**". The specification teaches that cells comprising an amplification at 20q13.2 are typically neoplastic. Thus, the identification of such amplifications reveals the presence of neoplastic cells.

The Examiner has offered no evidence to indicate that cells comprising the recited amplification are not neoplastic. Lacking such evidence, the Examiner has failed to establish that the method as recited in the claims would require undue experimentation. The Examiner has therefore failed to make her *prima facie* case under 35 U.S.C. §112, first paragraph, and this rejection should be withdrawn.

Moreover, the Examiner is reminded that whether undue experimentation is required by one skilled in the art is typically determined by reference to eight factors considered relevant to the inquiry: (1) quantity of experimentation necessary; (2) amount of guidance presented; (3) presence of working examples; (4) nature of the invention; (5) state of the prior art; (6) relative skill of those in the art; (7) predictability of the art; and (8) breadth of the claims. *In re Wands,* 8 USPQ2d 1400 (Fed. Cir. 1988) *citing Ex parte Forman Inc.,* 230 USPQ 546 (BPAI 1986).

In the instant case, essentially no experimentation is necessary (Wands Factor 1). The claimed method is easily and routinely performed by one of skill in the art. Considerable guidance is provided by the presence of working examples (Wands Factors 2 and 3). The nature of the invention is quite straightforward, being a simple nucleic acid-based assay. The prior art is well developed with respect to the use of hybridization-based assays (Wands Factor 5). The relative skill in the art is high, typically Ph.D. (Wands Factor 6). In view of the teachings provided in the application establishing that cells having the 20q13.2 amplification are typically neoplastic, the predictability of the art is high. The breadth of the claims is relatively narrow, being directed to a relatively simple hybridization assay.

Thus, when analyzed in light of *In re Wands*, practice of claims 26, 28, 37, 56, and 61-63 does not require undue experimentation and the rejection of these claims under 35 U.S.C. §112, first paragraph, should be withdrawn.

35 U.S.C. §102.

Claims 26, 56, and 61-63 were rejected under 35 U.S.C. §102 as allegedly anticipated by Morris *et al.* (1990) *Cytogenet. Cell Genet.,* 53; 196-200. In particular the Examiner alleged that the probe taught by Morris *et al.* is 88% similar to SEQ ID NO: 9. The Examiner further asserted that

> [A]lthough Morris et al do not mention determining an increased copy number of nucleic acid sequences at chromosomal region 20q13.2 the method taught by Morris et al. would **inherently** show an increased copy number of nucleic acid sequences at chromosomal region 20q13.2. [emphasis added] (Office Action, page 4, lines 12-13)

Applicants respectfully traverse. The Examiner is reminded that anticipation by inherency requires that:

1) the missing descriptive matter be "**necessarily present**" in the prior art reference and that

2) **it would be so recognized** by persons of ordinary skill in the art. [emphasis added] *Continental Can Co. v Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991)

In the instant case the Examiner has failed to meet both requirements to make a §102 rejection based on inherency. First, the Examiner has failed to establish that the Morris *et al.* probe would hybridize under the stringent conditions recited in claim 26.

In addition, even assuming *arguendo* that the Morris *et al.* probe would so hybridize, the Examiner has failed to establish that the missing descriptive matter:

> [D]etecting the formation of a hybridization complex to determine **the relative copy number of a nucleic acid in chromosomal region 20q13.2, thereby identifying** the presence or absence of neoplastic cells having an increased copy number of nucleic acid sequences at chromosomal region 20q13.2.

would **necessarily be present** and be **so recognized**. As explained in the previous response, the Morris *et al.* paper pertains to the discovery of a translocation between chromosome 5 and chromosome 22. **This reference lacks any description or mention whatsoever of chromosome 20.**

Even if, as argued by the Examiner, the Morris et al. probe hybridized to chromosome 22, there is no teaching in Morris *et al.* that would lead one to understand that such a hybridization would necessarily be detected nor that a copy number of a 20q13 hybridization would be assayed. To the contrary, the Morris *et al.* reference, being concerned only with chromosome 22 and chromosome 5 actually leads one of skill away from the presently claimed invention and is insufficient to support a rejection on principles of inherency. Accordingly, the rejection of claims 26, 56, and 61-63 under 35 U.S.C. §102 should be withdrawn.

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 337-7871.

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Respectfully submitted,

Tom Hunter
Reg. No: 38,498

APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE IN 08/785,532 WITH ENTRY OF THIS AMENDMENT

In the claims:

26. A method of detecting **in a sample** the presence or absence of neoplastic cells **having an increased copy number of nucleic acid sequences at chromosome region 20q13.2 [in a sample having an increased copy number of nucleic acid sequences at chromosome region 20q13.2]**, the method comprising:

contacting a nucleic acid sample from a human patient with a probe which hybridizes to a target polynucleotide sequence under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes, the target polynucleotide sequence comprising a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, and SEQ ID NO:13 wherein the probe is contacted with the sample under conditions in which the probe hybridizes selectively with the target polynucleotide sequence to form a stable hybridization complex; and

detecting the formation of a hybridization complex to determine **the relative copy number of a nucleic acid in chromosomal region 20q13.2, thereby identifying** the presence or absence of neoplastic cells having an increased copy number of nucleic acid sequences at chromosomal region 20q13.2.

APPENDIX B

CLAIMS PENDING IN USSN 08/785,532 WITH ENTRY OF THIS AMENDMENT

26. A method of detecting in a sample the presence or absence of neoplastic cells having an increased copy number of nucleic acid sequences at chromosome region 20q13.2, the method comprising:

contacting a nucleic acid sample from a human patient with a probe which hybridizes to a target polynucleotide sequence under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes, the target polynucleotide sequence comprising a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, and SEQ ID NO:13 wherein the probe is contacted with the sample under conditions in which the probe hybridizes selectively with the target polynucleotide sequence to form a stable hybridization complex; and

detecting the formation of a hybridization complex to determine the relative copy number of a nucleic acid in chromosomal region 20q13.2, thereby identifying the presence or absence of neoplastic cells having an increased copy number of nucleic acid sequences at chromosomal region 20q13.2.

27. The method of claim 26, wherein the nucleic acid sample is from a patient with breast cancer.

28. The method of claim 26, wherein the nucleic acid sample is a metaphase spread or a interphase nucleus.

29. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:1.

30. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:2.

31. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:3.

32. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:4.

33. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:5.

34. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:6.

35. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:7.

36. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:8.

37. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:9.

38. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:10.

39. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:12.

40. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:45.

48. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:1 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

49. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:2 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

50. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:3 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

51. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:4 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

52. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:5 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

53. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:6 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

54. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:7 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

55. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:8 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

56. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:9 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

57. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:10 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

58. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:11 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

59. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:12 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

60. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:45 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

61. The method of claim 26, wherein the probe is labeled.

62. The method of claim 61, wherein the label is a fluorescent label.

63. The method of claim 26, wherein the nucleic acid sample is a chromosome sample.

I hereby certify that this correspondence is being sent by the U.S. Postal Service via U.S. Mail to: Assistant Commissioner for Patents, Washington, D.C. 20231, on July 30, 2001

LAW OFFICES OF JONATHAN ALAN QUINE
By Richard Pask
RICHARD PASK

Attorney Docket No: M-8957-2US
Client Ref. No: 96-185-3

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re :
Application No.: **08/785,532**

Filed: **01/17/1997**

For: **Genes from the 20Q13 Amplicon and Their Uses**

REVOCATION AND SUBSTITUTION OF POWER OF ATTORNEY UNDER 37 CFR § 1.36

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Pursuant to 37 CFR § 1.36, The Regents of the University of California revoke(s) all previous powers of attorney and hereby appoints the attorneys and agents at Customer Number 22798 to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. The attorneys and agents at Customer Number 22798 include:

Jonathan Alan Quine, Ph.D., Reg. No. 41,261; Stacy Landry, Ph.D., Reg. No. 42,779; Christopher C. Sappenfield, Reg. No. 45,073; Gwynedd Warren, Reg. No. 45,200; Angela P. Horne, Reg. No. 41,079, Tom Hunter, Reg. No. 38,498, Emily M. Haliday, Reg. No. 38,903, and Stephen J. LeBlanc, Reg. No. 36,579.

Please direct all future correspondence regarding the subject application to CUSTOMER NUMBER 22798, that is:

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Paper # 25

The Regents of the University of California is the Assignee of record of the entire interest of the subject application.

The Regents of the University of California

Date: April 18, 2001

By: Linda S Stevenson
Name: Linda S. Stevenson
Title: Manager, Patent Prosecution